CHAPTER II.8. COST OF BLADDER CANCER

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CHAPTER II.8. COST OF BLADDER CANCER

II.8.A Background

This chapter contains a discussion of the methods used and results of estimating the direct medical costs incurred by bladder cancer patients. It does not include information on elements such as indirect medical costs, pain and suffering, lost time of unpaid caregivers, etc. The reader is referred to Chapter I.1 for a discussion of the cost estimation methods and cost elements that are relevant to all benefits estimates. In addition, Chapter II.1 contains information regarding cancer causality, a list of known and suspected carcinogens, and information on cancer cost estimation.

The costs presented in this chapter were current in the year the chapter was written. They can be updated using inflation factors accessible by clicking on the sidebar at left.

Link to Chapters I.1 and II.1
Link to inflation factors

II.8.A.1. Description

Bladder cancers are tumors that arise from the transitional cell lining of the urinary tract. These are a part of a larger group of tumors that are all related and are referred to as urothelial cell cancers. Urothelial cell cancers may occur in the kidneys, ureter, bladder, urethra, and the ducts of the prostate. The most common of these, bladder cancer, is the only cancer discussed in this chapter. Ninety percent of urothelial cell tumors are transitional cell carcinomas, with the remainder composed of squamous cell carcinomas and adenocarcinomas (Bennett and Plum, 1996).

Although a small percentage of bladder cancers differ somewhat from the majority in their cell origin or composition, this chapter contains an evaluation of all types of bladder cancer in aggregate. In addition, most risk assessments that would be used in evaluating benefits do not specify the type of bladder cancer. If a specific type of bladder cancer is of concern, Bennett and Plum (1996) may be consulted for additional information regarding prognostic information and treatment; however, the quantitative data are limited.

Bladder cancer is a common cause of cancer death in men and women in the U.S. (Feld et al., 1995), accounting for two percent of all cancer cases in the U.S.(Abeloff et al., 1995). Approximately 51,200 cases of bladder cancer were diagnosed in 1994 in the United States; approximately 10,600 bladder cancer deaths occurred in that year (Bennett and Plum, 1996). In

1996 the incidence rate was 27.7 per 100,000 in men and 7.4 in women (NCI, 1999).[1] The highest risk group are white men over the age of 64, who have an incidence rate of 217.8 per 100,000 (NCI, 1999).

The incidence of bladder cancer has increased overall by 7.7 percent between 1973 and 1996, due primarily to a 14.5 percent increase among those over the age of 64. The most dramatic increase has occurred among women, with a 22.6 percent increase in white women and a 24.8 percent increase among black women.[2] As discussed under "causality" below, this increase may be due to the increased rate of smoking among women. Incidence rates among black and white men over the age of 65 during the 1973 to 1996 interval have also increased substantially: 24.0 and 22.6 percent, respectively. Fortunately, this trend toward increased incidence has turned around slightly in very recent years (1992-1996) (NCI, 1999).

During the period 1973 to 1996, there has been a small drop in the incidence of bladder cancer among those under the age of 65 years (3.4 percent), driven solely by a decline in bladder cancer among white men and black women under the age of 65 years. Mortality rates have also decreased (discussed under prognosis, below).

Bladder cancer is observed in three times as many men as women. As with most cancers, it also occurs with much greater frequency among the elderly. The average age at diagnosis is between 70 and 75 years. Less than 1.6 percent of bladder cancers are diagnosed before the age of 40, and 21.7 percent are diagnosed over the age of 85 (NCI, 1999). The age distribution at diagnosis of bladder cancer is shown in Figure II.8-1. The steep incline in the probability of bladder cancer diagnosis with age is clear in this diagram. The data used to generate Figure II.8-1 are shown in Table II.8-1. The cumulative percents of bladder cancer at various ages were calculated using the population-weighted distribution of occurrence; these are also shown in Table II.8-1. The age-specific incidence data were used in the Section II.8.B medical cost calculations.

[1] Data on incidence and age at diagnosis were obtained from the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) reports and tables. These data were obtained online through the NCI web site at: http://www-seer.ims.nci.nih.gov in 1999.

[2] Racial designations are listed as specified by NCI.

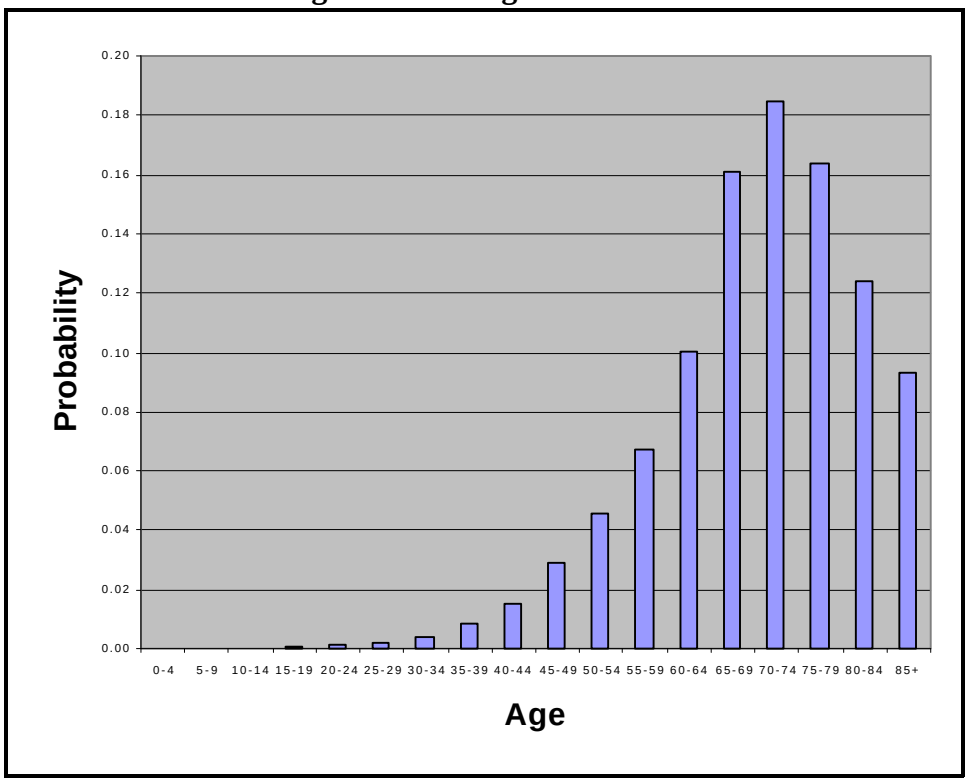
Table II.8-1. Age-specific Incidence of Bladder Cancer			
Age Group	**Age-specific Rate of Diagnosis Per 100,000**	**Percent of All Bladder Cancer Occurring in Age Group**	**Cumulative Percent of Bladder Cancer**
0 - 14	0.0	0.0	0.0
15 - 34	0.5	0.8	0.8
35 - 39	2.0	0.8	1.6
40 - 44	4.0	1.5	3.1
45 - 49	9.0	2.9	6.0
50 - 54	18.1	4.6	10.6
55 - 59	32.2	6.7	17.3
60 - 64	51.9	10.0	27.3
65 - 69	84.4	16.1	43.4
70 - 74	110.7	18.5	61.9
75 - 79	130.2	16.4	78.3
80 - 84	148.8	12.4	90.7
85+	138.2	9.3	100.0
Based on NCI, 1999			

II.8.A.2. Concurrent Effects

As with all cancers, bladder cancer may spread to other organs. In addition, treatment of cancer, which usually includes chemotherapy, radiation, and surgery, has numerous adverse side effects and may, in itself, lead to death. This is particularly true of the agents used to treat bladder cancer (Abeloff et al., 1995). Radiation treatments of cancer have led to increased risks of other types of cancer, sterility, etc. Surgery, especially the removal of a bladder, may cause long-term changes in health status, including reduced capacity or increased susceptibility to respiratory disease that may lead to death. These effects are associated with additional medical costs are considered in this chapter if they occur during the treatment period.[3]

[3] The source of direct medical costs for this chapter (Baker et al., 1979 and 1981) include all medical costs for cancer patients, minus usual background medical costs. This incremental approach allows for the inclusion of medical costs that are associated with treatment and side effects, and discussed in more detail in Section B.

Figure II.8.1. Age Distribution of Bladder Cancer



Bladder cancer has multiple concurrent symptoms that require treatment in addition to the treatments directed at the primary medical goal of cancer eradication. Many of these additional symptoms are related to chemotherapy. Effects observed include: hematuria (blood in urine) and irritative bladder symptoms, bladder obstruction leading to hydronephrosis, tumor infiltration of regional nerves or bone causing pain, and lymphedema as a result of lymphatic obstruction due to lymph node metastasis (Bennett and Plum, 1996; Abeloff et al., 1995), increased risk of epididymitis, orchitis (male reproductive disorders), pneumonitis, hepatitis, and sepsis (Abeloff et al., 1995).

There is a strong link between bladder cancer and smoking. Bladder cancer patients are much more likely to have smoked than people who have not been diagnosed with bladder cancer (causality is discussed below). Smoking is also associated with increased risks of many other diseases, including other cancers. There is no indication, however, that bladder cancer *causes* these other diseases. The simultaneous or sequential occurrence of the diseases are likely due to their common causal link to smoking.

The same pollutants that cause bladder cancer may cause other adverse effects, especially of the urogenital system. These effects can incur added medical costs not considered in this chapter. The risk assessment that serves as the basis for a benefits evaluation should include all adverse effects anticipated to result from exposure to the agent of interest.

II.8.A.3. Causality & Special Susceptibilities

The causality and progression of this disease are not fully understood. It has been hypothesized that bladder cancer may develop from a preneoplastic and preinvasive localized condition to hyperplasia and then to atypical hyperplasia and dysplasia. In some cases, the pathology progresses further to neoplasms (Abeloff et al., 1995). As discussed below, chemical irritants and other irritants are associated with bladder cancer and may cause the observed cell proliferation and hyperplasia, as well as the sometimes observed sequelae — bladder cancer. Experimental evidence suggests that the DNA-damaging effects of carcinogens on the urothelium causes cell proliferation. When the body is unable to repair DNA adequately, progression to bladder cancer may occur. For more detailed information on this topic see Abeloff et al. (1995).

Bladder cancer has been associated with environmental exposures for more than 100 years. Exposure to aromatic amines and working in the dye industry (especially with 2-naphthylamine) were known to cause high rates of bladder cancer among workers. More recently, workers in the rubber, electric, cable, paint, and textile industries had substantially higher incidences of bladder cancer, with exposures to benzidine, auramine, and 4-nitrophenol (Bennett and Plum, 1996), and arylamines from cigarettes and other sources (Jones and Ross, 1999) were particularly noted. Arsenic is also known to increase bladder cancer occurrence (ATSDR, 1998). It is difficult to identify exposures that result in bladder cancer because the latency period is between 15 and 50 years (Abeloff et al., 1995).

As noted above, cigarette smoking is also associated with a higher bladder cancer risk and may account for one-half of all cases (Bennett and Plum, 1996; Abeloff et al., 1995). The prevalence of smoking and occupational exposure among men may account for some or all of the increased incidence seen in men versus women. The dramatic increases in bladder cancer among women in recent years may be due to the relatively recent entrance of women into the workforce, and their recent increase in tobacco use. These factors would result in bladder cancer rates that are only recently observed to increase, due to the long latency of most solid tumors and the typically elderly age of diagnosis for bladder cancer.

In other parts of the world, infection with Schistosoma haemotobium is responsible for a large proportion of bladder cancer cases in less-developed countries (e.g., as studied in Egypt (Abeloff et al., 1995; Bennett and Plum, 1996)). Pharmaceuticals, including cyclophosphamide used in treating malignancies, and the analgesic phenacetin, are also associated with increased bladder cancer risk (Bennett and Plum, 1996; Abeloff et al., 1995).

Although genetic abnormalities are associated with bladder cancer, it is not clear wither these occurred as a result of the disease (or biomarker) or preceded the disease. Chromosome 9 abnormalities, particularly monosomy, occurs early in bladder cancer. 11p and 18p abnormalities are found in more advanced tumors (Bennett and Plum, 1996). For a more complete discussion of cellular-level changes and genetic markers for bladder cancer, see Jones and Ross (1999) and Abeloff et al. (1995). Individuals with a family history of bladder cancer before the age of 45 have a risk that is approximately 50 percent greater than the general population risk (Abeloff et al., 1995). Other genetic risks are suggested by data regarding cigarette smokers. Some individuals who detoxify cigarette toxins more slowly are theorized to have higher risks associated with smoking (Abeloff et al., 1995).

Other factors that may increase the risk of bladder cancer are chronic bladder irritation, bladder infections, and urinary nitrites (Abeloff et al., 1995).

Table II.1-1 in Chapter II contains a list of many of the chemicals known to cause or suspected of causing cancer (as reported in the EPA databases IRIS, HEAST, and HSDB). Most chemicals in the table were carcinogenic in animal studies. These studies do not provide organ-specific data because it is not generally assumed that cancer induction will necessarily occur at the same site in humans as in animals. Consequently, the chemicals listed in Table II-1 may cause bladder cancer and/or other types of cancer. Evaluation of the likelihood of this occurrence would require additional research (e.g., risk assessment).

Link to Table II.1-1

Bladder cancer is much more prevalent in the United States and in Spain than in many other countries. Rates here are 25 to 30 cases per 100,000, in contrast with a baseline rate of 2 per 100,000 in a typical low-rate area (Bennett and Plum, 1996). Bladder cancer also has a positive association with socioeconomic status (Jones and Ross, 1999; Abeloff et al., 1995), which has not yet been explained.

NCI provides age-, sex-, and race-specific data regarding diagnosis of bladder cancer from 1990 to 1994, which may be used to evaluate susceptibilities among population subgroups. The data must be used with care because diagnostic rates indicate occurrence only, and may or may not indicate differences in susceptibility. See Chapter I.1 for a more detailed discussion of susceptibilities.

Link to Chapter I.1

II.8.A.4. Treatments and Services

As noted above, bladder cancer is usually treated with surgery, chemotherapy, and/or radiation, depending on the type of bladder cancer, the stage of cancer at diagnosis, patient health, and other factors. The treatment of bladder cancer can be defined more precisely by histologic type and specific location of the cancer in the bladder. In this analysis, which is concerned with the average cost for all bladder cancers, all histologic types and sub-sites are considered together.

Treatment is carried out in phases including initial diagnosis, initial treatment, follow-up and maintenance treatment, and, for those who do not survive, terminal treatment and palliative care. Although there are some components of each treatment that are unique to each phase, most medical activities and services may occur more than once over the course of the disease from diagnosis to death or cure. For example, X-rays may be used in diagnosis, to provide ongoing status updates, to assist in determining initial and subsequent surgical and other treatment interventions, etc.

Initial diagnostic activities may include an evaluation of signs and symptoms, abdominal, pelvic, bone, and chest scans, intravenous pyelogram, cystoscopy, urinary cytology, computed tomography (CT) scans, magnetic resonance imagery (MRI), biopsies, and other procedures (Bennett and Plum, 1996; Abeloff et al., 1995). Staging of the disease occurs during this phase and is critical to determination of subsequent medical actions. Most tumors are confined to the transitional cell layer and these are generally treated only with surgery. The tumors often recur, which requires frequent cystoscopy with subsequent removal of recurrent tumors as necessary. Higher-grade tumors require chemotherapy or immunotherapy. Invasive cancers with a higher metastatic potential often require total removal of the bladder, and subsequent reconstruction of an alternative urinary reservoir (Bennett and Plum, 1996)

Although there is an 80 to 90 percent survival rate among bladder cancer patients during initial diagnosis and treatment, tumors recur in 30 to 80 percent of patients, and 30 percent progress to a higher stage or grade. Often chemotherapy is used to control or prevent this progression; however, this entails the use of chemicals that are toxic to other organ systems (Abeloff et al., 1995). Photodynamic therapy has also been used recently with success, without the chemically-induced side effects (Abeloff et al., 1995).

The small percentage of patients who cannot be cured receive terminal care, which may include a variety of medical services, long-term care in a nursing facility, palliative care, family counseling, etc.

II.8.A.5. Prognosis

II.8.A.5.1 Background

The prognosis for bladder cancer is relatively good, compared to many cancers. Approximately 26 percent of patients with bladder cancer die of the disease.[4] Mortality rates for bladder cancer patients have decreased overall by 24 percent from 1973 to 1996. The most dramatic improvements have been made among blacks under the age of 65 years, with a 46.5 percent reduction in mortality among those diagnosed with the disease (NCI, 1999). Improvements in survival are due to both better diagnostic methods and improved treatments.

The overall prognosis for bladder cancer patients is good, with an average of only 19 percent of patients dying of the disease within five years. Among younger patients the survival rates are better, with those diagnosed under the age of 45 having a 7.9 percent mortality rate over the first five years post-diagnosis. Those with more limited tumors have a much better prognosis than those with metastatic tumors (discussed below), with a range of 6.9 percent mortality with localized tumors to 93.6 percent mortality among those with distant tumors (based on 1989 to 1995 data) (NCI, 1999).

Tumors that are restricted to a single site, or that occur in multiple sites within the bladder, provide the best prognosis. Most bladder cancer cases are superficial tumors of the transitional cell layer with a low potential for metastatic spread. Those that invade multiple layers of the organ wall and/or metastasize to other organs yield a poorer prognosis. Death occurs primarily as a result of uncontrolled growth of metastatic tumors.

A dynamic observed with bladder cancer, but not common to cancers, is a long-term increase in mortality over 20+ years. Most cancers cause high rates of mortality during the first few years, but are often considered "cured" if the patient survives without recurrence of the cancer for five years. Based on National Cancer Institute (NCI) statistics, bladder cancer continued to cause increased mortality for at least 20 years (the maximum length tracked) post-diagnosis. This trend is discussed in more detail below.

II.8.A.5.2 Relative Survival Rates (RSRs)

The NCI Surveillance, Epidemiology, and End Results (SEER) data reports were accessed online to obtain information regarding mortality and survival probabilities and the duration after diagnosis until death (NCI, 1999). Basic survival statistics on bladder cancer are provided in this

[4] This value is relevant for patients diagnosed at the age of 70 years (the average age of diagnosis for bladder cancer) and is based on a follow-up period of 20 years. The method of calculating this value is discussed below in Section II.8.A.5.2, and source values are listed in column (6) of Table II.8-3.

section because they relate to prognosis. Methods used to convert the NCI statistics to survival probabilities are discussed briefly in this section and in detail in Chapter II.2 on stomach cancer.

Link to Chapter II.2

NCI provides the relative survival rate (RSR) for each year post-diagnosis. The RSR is the number of observed survivors among these patients, divided by the number of "expected" survivors among persons with the same age and gender in the general population (observed/expected). The equation for this is:

$$RSR = \frac{observed\ survival\ rate\ among\ bladder\ cancer\ patients}{survival\ rate\ among\ age-\ and\ sex-matched\ cohort\ in\ the\ general\ population}$$

The RSR takes into account that there are competing causes of death that increase with age. The RSR for bladder cancer patients during the first year post-diagnosis is 0.86 (NCI, 1999). This value indicates that a person with bladder cancer would have, on average, a one-year survival probability that is 86 percent of someone of the same age and gender in the general population. The RSRs provided by NCI for each year post-diagnosis are averages obtained from all ages at diagnosis.

An evaluation of the RSRs for bladder cancer over the past 20 years indicates that (1) survival has increased notably (up to ten percent) over the 20 years, and (2) mortality from bladder cancer, while at much lower rates than for some other cancers, continues at non-negligible rates for at least 20 years post-diagnosis. This trend differs from other cancer evaluations previously carried out for this handbook. Due to the long-term dynamic of increasing mortality for bladder cancer, the medical and opportunity costs incurred by bladder cancer patients were estimated for 20 years post-diagnosis (previous chapters considered ten years).

Because the RSRs for many years (e.g., 20 years) post-diagnosis incorporate the survival probabilities of bladder cancer patients who were diagnosed many years ago (e.g., in 1975), direct reliance on the RSRs provided by NCI will result in downward-biased estimates of what RSRs would be for patients who are *currently* being diagnosed with bladder cancer. This bias occurs because the RSRs at each year post-diagnosis are currently significantly higher than they were many years ago (i.e., the survival for years one through five post-diagnosis in the late 1980s is higher than for years one though five in the 1970s).

To provide a more accurate estimate of what the RSRs (and the corresponding survival and mortality probabilities) for bladder cancer patients are likely to be for the next 20 years, we estimated RSRs for each

year post-diagnosis using a two-step procedure. This procedure focuses on using the most current data available for each year post-diagnosis. In the first step, we assumed that the ratio of the RSR at *n* years post-diagnosis to the RSR at ($n-1$) years post-diagnosis in the most recent year for which we have data is what that ratio will be in future years. For example, the most recent year for which we have an RSR for one year post-diagnosis for bladder cancer is 1995. The RSR in 1995 is 0.91, which we assume will be the RSR for one year post-diagnosis in future years. The most recent year for which there is an RSR for two years post-diagnosis is 1994. We assume that:

$$\frac{RSR_2^{1994}}{RSR_1^{1994}} = \frac{RSR_2^{future}}{RSR_1^{future}}$$

so that

$$RSR_2^{future} = RSR_1^{future} \times \frac{RSR_2^{1994}}{RSR_1^{1994}} \ .$$

Using the most recent RSR for one year post-diagnosis (0.91), and the RSRs we have from 1994 for one year and two years post-diagnosis (0.911 and 0.865, respectively), the RSR for two years post-diagnosis is estimated to be $0.91 \times (0.865/0.911) = 0.8641$. This estimate of the RSR for two years post-diagnosis is then used to estimate the RSR for three years post-diagnosis, using the above formula. We continue this process until we have generated RSRs for each of twenty years post-diagnosis.

The RSRs, derived as described above, are only *estimates* of the underlying population RSRs (i.e., the RSRs for the entire population of bladder cancer patients in the United States). As such, they display some of the "bumpiness" that data often contain. In step two, a plot of these estimated RSRs against years post-diagnosis was generated. It shows that they follow a general exponential decay trend. Rather than use these estimated RSRs, regression was used to estimate the smooth trend described by the estimates derived in step one. In particular, we estimated the model:

$$\ln(RSR) = a + b \times \ln(\text{years post-diagnosis})$$

using the RSRs estimated in step one. The intercept (a) was estimated to be -0.131866 and the slope (b) was estimated to be -0.0134114. The fit was excellent, with an R^2 of 0.952. Exponentiating the predicted natural logarithms of RSR yielded the predicted RSRs shown in Table II.8-2.[5]

[5] All vital statistics data in this document applicable to the general population were obtained from the National Center for Health Statistics (NCHS) Vital Statistics in the United States (NCHS, 1993).

Some bladder cancer patients will die of bladder cancer, but most die of other causes. The probability of a bladder cancer patient dying of causes other than bladder cancer cannot be assumed to be the same as the probability of someone in the general population dying of other causes, particularly in the first few years post-diagnosis, when a bladder cancer patient's probability of dying of bladder cancer is not trivial.[6] This becomes clear in the extreme case in which the probability of dying of an illness is extremely high. Suppose, for example, that the probability of dying of all causes except for illness X is 0.025 in the general population. Suppose that in a cohort of patients diagnosed with illness X the probability of dying from illness X in the first year post-diagnosis is 0.99. If dying of other causes in this cohort were the same as in the general population (0.025), then their probability of dying would be greater than 1.0.

[6] This difference becomes clear in the extreme case in which the probability of dying of an illness is extremely high. Suppose, for example, that the probability of dying of all causes except for illness X is 0.025 in the general population. Suppose that in a cohort of patients diagnosed with illness X, the probability of dying from illness X in the first year post-diagnosis is 0.99. If the probability of dying of other causes in this cohort were the same as in the general population (0.025), then the probability of someone in the cohort dying would be greater than 1.0.

Table II.8-2. Estimated RSRs* for Bladder Cancer for the First 20 Years Post Diagnosis	
Years Post-Diagnosis (n)	**Estimated RSR for n Years Post-Diagnosis**
1	0.86
2	0.85
3	0.84
4	0.83
5	0.82
6	0.81
7	0.80
8	0.79
9	0.78
10	0.77
11	0.76
12	0.75
13	0.74
14	0.73
15	0.72
16	0.71
17	0.70
18	0.69
19	0.68
20	0.67
*The estimated RSR for each year post-diagnosis is the result of a two step procedure, using the set of RSRs reported by NCI (1999), as described in the text above.	

The probability of a bladder cancer patient dying of bladder cancer and the probability of a bladder cancer patient dying of some cause other than bladder cancer in the *n*th year post-diagnosis, given survival to the *n*th year, were each derived from two known probabilities:

1) the probability of a bladder cancer patient surviving through the *n*th year post-diagnosis, given survival to the *n*th year; and
(2) the probability of dying of causes other than bladder cancer in a matched cohort in the general population.

The derivation is explained in detail in the Appendix to Chapter II.2.

Link to Chapter II.2, Appendix II.2-A

Because each of the known probabilities depends on the number of years post-diagnosis and (minimally) on age at diagnosis, the derived

probabilities were calculated for each of the 20 years post-diagnosis and for the average age at diagnosis (70 years).[7] The following probabilities are shown in Table II.8-3:

1) survival through the *n*th year,
2) dying of bladder cancer during the *n*th year, and
3) dying of some other cause during the *n*th year.

Probabilities of survival and dying of all causes among all members of the general population aged 70 were obtained from the National Center for Health Statistics (NCHS) Vital Statistics in the United States (NCHS, 1993). They are also shown in Table II.8-3. The values in this table are used in Section II.8.B to calculate the expected medical costs of bladder cancer patients. The probabilities in the general population of dying from bladder cancer are 0.00020 in the 70-74 year age group, 0.00031 in the 75-79 year age group, 0.00047 in the 80-84 year age group, and 0.00069 in the 85+ age group. The probabilities in column (3) were derived by subtracting these probabilities from the corresponding probabilities of dying from any cause in the *n*th year, given survival to the *n*th year. The Chapter II.2 Appendix contains a detailed explaination of the derivation of survival and mortality probabilities.

Link to Chapter II.2, Appendix II.2-A

The mortality rate of 26 percent, cited in the introduction to this section, was calculated for patients who are diagnosed at age 70 as the sum of the probabilities of their dying of the disease in each year post-diagnosis. This rate was calculated for 20 years post-diagnosis, using the data shown in Table II.8-3. The probabilities of dying of bladder cancer during each year post-diagnosis, shown in the column titled "probability of dying of bladder cancer in the *n*th year post-diagnosis" were summed to obtain a value of 26 percent.

[7] Twenty years is period that captures most of the deaths due to bladder cancer among those diagnosed with the disease. This period is a reasonable maximum duration of maintenance care and treatment for those who do not die of bladder cancer.

Table II.8-3. Survival and Mortality Probabilities for the Average Bladder Cancer Patient[a]						
	A Cohort in the General Population (Matched)		A Cohort of Bladder Cancer Patients			
Years post-diagnosis (n)	Probability of surviving *n* years	Probability of dying in *n*th year of causes other than bladder cancer, given survival to the *n*th year	Relative Survival Rate (RSR)	Probability of surviving through the *n*th year post-diagnosis	Probability of dying of bladder cancer in the *n*th year post-diagnosis[b]	Probability of dying of other causes in the *n*th year post-diagnosis
0	1.000	---	---	1.0	---	---
1	.973	.027	0.86	.842	.134	.025
2	.945	.029	0.85	.806	.011	.024
3	.915	.031	0.84	.771	.011	.025
4	.884	.034	0.83	.735	.010	.026
5	.852	.037	0.82	.698	.010	.027
6	.817	.040	0.81	.661	.009	.028
7	.782	.043	0.80	.624	.009	.028
8	.745	.047	0.79	.586	.008	.029
9	.707	.051	0.78	.549	.008	.030
10	.667	.056	0.77	.511	.007	.030
11	.626	.061	0.76	.473	.007	.031
12	.584	.067	0.75	.436	.006	.031
13	.541	.073	0.74	.398	.006	.032
14	.497	.081	0.73	.361	.005	.032
15	.451	.090	0.72	.324	.005	.032
16	.410	.090	0.71	.290	.004	.029
17	.373	.090	0.70	.260	.004	.026
18	.339	.090	0.69	.234	.004	.023
19	.308	.090	0.68	.210	.003	.021
20	.280	.090	0.67	.188	.003	.019

a. The survival and mortality probabilities for bladder cancer patients presented here are derived from the RSRs estimated from RSRs obtained from NCI and the survival probabilities for a matched cohort in the general population. The average age of diagnosis of 70 years was used. See text for an explanation calculation methods.

b. When the probalities in this column are summed, they yield the probability of dying of bladder cancer over 20 years post-diagnosis, which is equal to 26 percent.

There is likely to be additional loss, although at a very low rate, beyond 20 years; however, data were not available on those values. Impacts beyond 20 years are unlikely to have a substantial impact on cost analyses because there are many competing causes of death when a person reaches 90 years of age.

The RSR can be used to approximate the probability of mortality at young ages, when the background death rate is minimal. The bladder cancer mortality rate is approximated by 1 – RSR when background age-related mortality from other causes is not considered. In the case of bladder cancer, the RSR is 0.67 and 1 - RSR = 0.33. In reality, there is always a background death rate in a population, and this rate increases with age. As noted previously, most bladder cancer patients do not die of bladder cancer. Only 18.8 percent of the population diagnosed with bladder cancer survive to 20 years post-diagnosis, but most of these losses are due to other causes of death than bladder cancer. The RSR, used with the background mortality rates of the population at the average age at diagnosis, provides clear information on the survival and mortality dynamic of that specific population. If the cancer occurs at a younger age than usual due to its genesis (e.g., chemical induction), however, then the mortality statistics obtained through the method described above will underestimate bladder cancer-related mortality. In these cases, the RSR itself is a better approximation of survival (and derived mortality), allowing estimation of mortality at young ages when background mortality is negligible.

Some environmentally-induced cancers, such as arsenic-induced skin cancer, occur at much younger ages than those at which the cancers are typically observed in the general population. Consequently, the use of the inverse of survival, 1 – RSR (e.g., 0.33 in the case of bladder cancer), as an estimate of mortality may be very relevant for calculating benefits associated with the avoidance of some environmentally-induced cancers. Due to the higher mortality estimates that this approach will always generate, the benefits of avoiding the disease will be larger when the RSR is used directly to estimate cancer mortality. When there is no evidence that the disease will occur at an age that is younger than that of the general population, the calculations that precede this — that link morbidity and mortality to the *average* age at diagnosis — are used to estimate direct medical costs.

II.8.B Costs of Treatments and Services

II.8.B.1. Methodology

II.8.B.1.1 Overview

There is no single typical case or treatment pattern for bladder cancer due to individual differences in the stage of cancer at diagnosis, multiple treatment options, patient health and age, and other factors; however, average costs can be calculated. Treatment of bladder cancer may occur over a brief or extended period of time, and costs may be limited or substantial. As discussed in Section II.8.A, bladder cancer has a relatively low mortality rate, with a relative survival rate of 0.67. The medical costs of those who die of the disease are usually very different than for those who survive (this is discussed in more detail in Chapter I.1). This chapter therefore provides costs for the "average" bladder cancer patient, as well as for survivors and nonsurvivors as separate patient groups.

Link to Chapter I.1

II.8.B.1.2 Medical Cost Data

II.8.B.1.2.1 Sources

Medical cost data would ideally be obtained on current medical expenditures. Although data files are maintained by public and private sector sources, they are not generally available for public use. In addition, to obtain reliable cost estimates it is necessary to evaluate very large databases of charges from a variety of sources. This method was neither practical nor cost-effective for the development of this chapter, given the availability of summary data from other sources. A data search was conducted to locate information in the medical economics literature regarding medical costs associated with bladder cancer. In addition to a literature search, most federal agencies dealing with cancer, disabilities, medical costs and their management, and related issues were contacted for information, and the various federal databases were discussed with senior staff at these agencies.

Very recent cost data were not located.[8] However, current (1994) cancer data were obtained regarding incidence and survival (as reported in Section II.8.A, above), and were used with cost data from the 1980s described below. The cost estimates presented in this section are based primarily on the work of Baker et al. (1989) and Hartunian et al. (1981), respectively, and on two sources of statistical data: the National Cancer Institute (1999) and Vital Statistics of the United States, 1993 (NCHS, 1997).

[8] Studies were located that used more recent cost data than those used in this analysis. Due to serious limitations (i.e., data were incomplete), the studies were not used. They are reported in the "Other Studies" section at the end of Section II.8.B.

Based on the 1997 review of the medical literature carried out for the development of this chapter, there do not appear to be widely-adopted new treatment methods for bladder cancer that alter either the medical costs or the survival rates for most patients substantially. Consequently, the cost estimates presented in this chapter may be considered appropriate under most circumstances (e.g., regional costs may vary).

II.8.B.1.2.2 Baker et al.'s Cost Estimation Method

Baker et al. (1989) used the Continuous Medicare History Sample File (CMHSF) to estimate the per-patient average lifetime medical cost of treating bladder cancer based on data files from 1974 to 1981. They chose CMHSF because:

1) it is a nationally representative sample of the Medicare population (five percent), covering over 1.6 million patients;
2) it is longitudinal, dating from 1974 to 1981; and
3) it captures the majority of medical expenses for each beneficiary.

Five Medicare files are included in the CMHSF, which cover:

1) inpatient hospital stays,
2) skilled nursing facility stays,
3) home health agency charges,
4) physicians' services, and
5) outpatient and other medical services.[9]

Costs not included are outpatient prescription medications and nursing home care below the skilled level.

Because CMHSF provides no indication of initial diagnosis, Baker et al. assumed that disease onset occurred when a diagnosis of bladder cancer was listed on a hospitalization record following a minimum of one year without a bladder cancer diagnosis. This assumption is reasonable due to the high frequency of hospitalization associated with the disease (i.e., individuals diagnosed with bladder cancer would be hospitalized). Only patients with an initial diagnosis during the years covered by the database (1974-1981) were included.

[9] See Baker et al. (1989 and 1991) for further details. Baker et al. (1991) contains additional descriptive data regarding the database and methods used for the cost analysis; however, it does not contain cost data for bladder cancer.

Costs associated with bladder cancer were assigned to three post-diagnostic time periods:

- initial treatment, during the first three months following diagnosis;
- maintenance care, between initial and terminal treatment; and
- terminal treatment during the final six months prior to death.

As noted in Chapter I.1, the amount paid for service may differ from the actual medical costs because many insurers and federal programs either 1) pay only a portion of total costs, or 2) pay more than actual costs to underwrite the care providers' losses due to underpayment from other sources.

Link to Chapter I.1

Baker et al. used provider charges, rather than Medicare reimbursements (which represent only a portion of most total charges), thus providing a more accurate cost estimate. To improve the accuracy of the cost estimates, Baker et al. included cost data on coinsurance, deductibles, and other cost components. They made four adjustments to the cost estimates calculated from the CMHSF. First, charges were added for skilled nursing facilities (SNFs) not covered by Medicare by multiplying the "length of stay" at an SNF (computed from admission and discharge dates) by the average daily SNF charge. Second, the annual Medicare Part B deductible of $60 was added to the reimbursed charges in the database. Third, since Medicare pays only 80 percent of physicians' charges, Baker et al. scaled these reimbursements to 100 percent of physicians' charges to better reflect social costs. Finally, they inflated all dollar values to 1984 dollars using the Medical Care component of the Consumer Price Index.

II.8.B.1.2.3 Cost Estimates by Treatment Period

Medical costs associated with the initial, maintenance, and terminal cancer care treatment periods were itemized in Baker et al. (1989) and are shown in Table II.8-4. The 1989 paper did not report incremental costs or the costs of other medical services, which would be anticipated to occur while the patient was receiving cancer treatment (i.e., co-morbidity/background costs). In order to estimate the incremental costs, a co-morbidity cost of $2,988 per year (1984 dollars) from Baker et al. (1991) was used in this analysis. (This is equivalent to $6,394 in 1996 dollars using the CPI multiplier of 2.14 for 1984 to 1996.) The co-morbidity cost was pro-rated for this analysis using the specified durations for the initial (three-month) and terminal (six-month) treatment periods.

Table II.8-4 lists the incremental costs calculated for the three treatment periods. Total costs are reported for the initial and terminal care periods. Annual costs for the maintenance period are shown and are further

discussed in the "Lifetime Costs" section below. Using the Medical Care component of the Consumer Price Index (CPI-U), all costs are inflated to 1996 dollars for purposes of this handbook. (The adjustment factor for 1984 to 1996 is 2.14; Bureau of Labor Statistics.)

Table II.8-4. Average Per Patient Costs for the Three Periods of Treatment for Bladder Cancer in 1996 dollars
Costs adjusted for inflation using the Medical Care component of the Consumer Price Index (CPI-U) 1996:1984 = 2.14 (Bureau of Labor)

Treatment Period	Incremental Cancer Treatment Cost
Initial (3 months)	$16,527
Maintenance (per year)	$13,277
Terminal (6 months)	$36,558

Based on Baker et al., 1989, with comorbidity charges from Baker et al., 1991.

II.8.B.1.3 Calculation of Lifetime Cost Estimates for the "Average" Bladder Cancer Patient

This section contains a discussion of the calculation of lifetime medical costs for the "average" bladder cancer patient. The sections that follow discuss methods and results of calculations for estimating costs for survivors and nonsurvivors of bladder cancer separately. These separate approaches were used to address specific requirements of different activities that EPA carries out using direct medical cost data. Although Baker et al. (1989) provide useful cost estimates for the three treatment periods, they do not provide information on two critical aspects of medical costs:

1) costs for survivors versus nonsurvivors of bladder cancer. These may differ substantially. For example, survivors would not have terminal care costs and may receive maintenance services for an extended time period.; and
2) estimates of the duration of the maintenance periods.

Data regarding age at diagnosis of bladder cancer were obtained from NCI (1999). Survival and mortality probabilities for each year post-diagnosis were derived from relative survival rates obtained from NCI (1999), as discussed in Section II.8.A.5.2.

Link to II.8.A.5.2

This information was used to address many time-related medical cost issues. For some aspects of the analysis, however, detailed information

was not available and average values have been used as a reasonable approximation (e.g., a 20-year maintenance period was assumed for survivors of bladder cancer). When average values or other assumptions are used in this analysis, they are so noted.

As previously noted, there are no substantial differences in survival related to age at diagnosis, and NCI does not provide age-specific relative survival rates for each year post-diagnosis. Consequently, it was assumed for this analysis that the relative survival rates for bladder cancer were the same for all ages. The survival and mortality probabilities for bladder cancer patients, which are incorporated into calculations of expected medical costs as discussed below, are based on this assumption.

The analysis assumes that death always occurs midyear. All bladder cancer patients are therefore assumed to incur the costs of initial treatment during the first three months of the illness. The costs incurred after that during the first year depend on whether the patient:

1) survives through the year,
2) dies of bladder cancer during the year, or
3) dies of some other cause during the year.

Patients who survive through the year incur the costs of initial treatment ($16,527.2) during the first three months, and then incur nine months' worth of maintenance care costs ($0.75 \times \$13,276.6 = \$9,957.4$) during the remainder of the year. The total cost incurred during the first year by those patients who survive the year is therefore $\$16,527.2 + \$9,957.4 = \$26,485$.

Bladder cancer patients who die of bladder cancer during the first year incur the initial treatment cost and then incur terminal care costs for the remaining three months of their lives (because those who die are assumed to die midyear). Total costs during the first year post-diagnosis in this case are therefore $\$16,527.2 + (0.5 \times \$36,557.6) = \$34,806$.

Finally, the small percentage of bladder cancer patients who die of causes other than bladder cancer during the first year post-diagnosis incur the initial treatment costs and then incur three months' worth of maintenance care costs. Total first-year costs for these patients are therefore $\$16,527.2 + 0.25 \times \$13,276.6 = \$19,846$.

The expected medical costs for bladder cancer patients during the first year post-diagnosis, then, may be expressed as:

> **Expected First-Year Cost: initial treatment costs + [maintenance care costs for nine months × probability of survival through first year + terminal care costs for three months × probability of dying of bladder cancer during first year + maintenance care costs for three months × probability of dying of other causes during the first year]**

Example: Expected first-year medical costs of a bladder cancer patient diagnosed at age 70

As noted above, all bladder cancer patients incur an initial treatment cost of $16,527. Those who survive through the year also incur maintenance care costs for the remaining three quarters of the year. The total first-year costs of those who survive the year are:

Initial treatment:	$16,527.2
Maintenance treatment:	$9,957.4 (.75 × $13,276.6)
Total First-Year Cost	$26,485

About nine percent of bladder cancer patients die of bladder cancer during the first year. Those who do will incur the initial treatment costs plus half of the terminal care costs. The total first-year costs of those who die of bladder cancer during the year are:

Initial treatment:	$16,527.2
Terminal care:	$18,278.8 (.50 × $36,557.6)
Total First-Year Cost	$34,806

Finally, a small percentage of patients will die of competing illnesses during the first year. Because those who die of causes other than bladder cancer are assumed to die at the midpoint of the year, costs during the first half of the year are assumed to consist of the initial treatment costs for three months, plus three months of maintenance care costs as follows:

Initial treatment:	$16,527.2
Maintenance treatment:	$3,319.1 (.25 × $13,276.6)
Total First-Year Cost	$19,846

For each subsequent year, costs consist entirely of maintenance care costs for those who survive the year. For those who do not survive the year, costs depend on whether death was due to bladder cancer or other causes.

For those who die of bladder cancer during the *n*th year, costs incurred that year consist of six months of terminal care costs, or $36,558. For those who die of other causes during the *n*th year, there are six months of maintenance care costs, or 0.5 × $13,276.6 = $6,638.

The expected first-year medical cost incurred by the "average" bladder cancer patient diagnosed at age 70 is a weighted average of the costs of those who survive the first year, those who die of bladder cancer during the first year, and those who die of other causes during the first year, where the weights are the probabilities of each of these occurrences.[10] The weighted average medical costs were calculated for 20 years post-diagnosis and expected costs were summed over the 20 years. This timeframe was assumed to be a reasonable period over which additional medical costs associated with bladder cancer (i.e., maintenance care costs) would be incurred by bladder cancer patients.

Although the actual average period of maintenance care for bladder cancer is not known, the resulting uncertainty about the expected maintenance costs during a 20-year period is somewhat lessened by the fact that a large percentage of bladder cancer patients diagnosed at age 70 die within the 20-year period (mostly of other causes), and would therefore not incur maintenance costs for the full 20 years anyway.

The expected medical costs for bladder cancer patients during the *n*th year post-diagnosis, for $n>1$, then, may be expressed as:

> **<u>Expected *n*th-Year (*n*>1) Cost:</u> [maintenance care cost for one year × probability of survival through *n*th year + terminal care cost for six months × probability of dying of bladder cancer during the *n*th year + maintenance care cost for six months × probability of dying of other causes during the *n*th year]**
>
> **<u>Expected Lifetime Cost</u> = Expected first-year cost + the sum of the (discounted) expected subsequent-year costs**

[10] Although this analysis focuses on costs incurred by a patient diagnosed with bladder cancer at the average age of diagnosis (70 years), some environmentally-induced cancers are diagnosed at earlier ages than those commonly reported for the cancers (e.g., arsenic-induced skin cancer). As noted in Section II.8.A, this earlier diagnosis has an impact on the mortality dynamics and on the direct medical costs. The uncertainty analysis contained in Section II.8.C includes an age-specific analysis of direct medical costs, that demonstrates the differences that can result in earlier ages of onset than those used in the basic analysis for this chapter.

The first year of treatment is calculated differently from other years because the first three months of that year are spent in "initial" treatment and the costs for that period of intensive medical care and surgery are calculated separately.

The mathematical equation for the expected lifetime medical costs incurred by the "average" bladder cancer patient over a 20-year period is:

$$\$16{,}527 + (\$13{,}277 \times 0.75 \times ps_1) + (\$13{,}277 \times 0.25 \times pm_1{}^{o}) + (\$36{,}558 \times 0.5 \times pm_1{}^{bc})$$

$$+\sum_{y=2}^{20}\left[(ps_y \times \frac{\$13{,}277}{(1+r)^{y-1}}) + (pm_y{}^{o} \times \frac{\$6{,}638}{(1+r)^{y-1}}) + (pm_y{}^{bc} \times \frac{\$36{,}558}{(1+r)^{(y-1)}})\right]$$

Where:

y	=	the year post-diagnosis,
ps	=	the probability of surviving through the year,
pm^{bc}	=	the probability of dying of bladder cancer during the year,
pm^{o}	=	the probability of dying from other causes during the year, and
r	=	the discount rate.

The cost estimates for each year post-diagnosis and the estimate of undiscounted expected total cost for a 20-year period are shown in Table II.8-5 for the "average" bladder cancer patient diagnosed at age 70. The survival and mortality probabilities necessary for the calculations of costs are shown in Table II.8-3.

Link to Table II.8-3

II.8.B.1.4 Calculation of Lifetime Cost Estimates Separately for Bladder Cancer Survivors and Nonsurvivors

II.8.B.1.4.1 Survivors and Nonsurvivors

As noted above, there are differences in medical services provided to bladder cancer patients who survive the disease (survivors) versus those who die of the disease (nonsurvivors). Based on cost estimates by Baker et al. (1989), terminal care is provided for approximately six months to terminally ill cancer patients. The costs to nonsurvivors for this care ($36,558) is considerably higher than costs for survivors who receive maintenance care for the same period of time ($6,638).[11]

EPA may use the value of a statistical life (VSL) for nonsurvivors and thus calculate separate costs for survivors and nonsurvivors. The method

[11] Nonsurvivors include only those who die of bladder cancer and do *not* include those who die of any other causes.

shown above to calculate costs for the "average" patient uses the unconditional probabilities of survival and mortality listed in Table II.8-3. The method used to calculate costs for survivors and nonsurvivors separately requires the probabilities that are conditional on being either a survivor or nonsurvivor of bladder cancer.

Link to Table II.8-3

The conditional probability of a bladder cancer nonsurvivor dying in the *n*th year is the number of nonsurviving bladder cancer patients who die of bladder cancer during the *n*th year divided by the total number of bladder cancer nonsurvivors. Likewise, the conditional probability of a bladder cancer survivor dying in the *n*th year is the number of bladder cancer survivors who die (of causes other than bladder cancer) during the *n*th year divided by the total number of bladder cancer survivors. A detailed explanation of the derivation of these values is provided in Chapter II.2. The conditional probabilities of survival and mortality for survivors and nonsurvivors of bladder cancer are given in Table II.8-6.

Link to Chapter II.2

II.8.B.1.4.2 Calculation of Lifetime Cost Estimates for Bladder Cancer Survivors

As shown in the example portion of Section II.8.B.1.3, cost estimates are calculated by summing the costs of the different treatment phases over the lifetime of the bladder cancer patient.

Link to Section II.8.B.1.3

Table II.8-5. Expected Costs of Medical Services (in 1996$) for Bladder Cancer Patients (Age of Onset = 70)[a]

	Medical Costs in the *n*th Year (undiscounted)			
Years Post-Diagnosis (n)	**if survive through the *n*th year**	**if die of bladder cancer in the *n*th year**	**if die of other causes in the *n*th year**	**Expected Medical Costs for the *n*th Year Post-Diagnosis[c] (Undiscounted)**
1[b]	26,485	34,806	19,846	27,432
2	13,277	36,558	6,638	11,276
3	13,277	36,558	6,638	10,790
4	13,277	36,558	6,638	10,299
5	13,277	36,558	6,638	9,802
6	13,277	36,558	6,638	9,301
7	13,277	36,558	6,638	8,794
8	13,277	36,558	6,638	8,283
9	13,277	36,558	6,638	7,769
10	13,277	36,558	6,638	7,254
11	13.277	36,558	6,638	6,740
12	13.277	36,558	6,638	6,224
13	13.277	36,558	6,638	5,708
14	13.277	36,558	6,638	5,195
15	13.277	36,558	6,638	4,685
16	13.277	36,558	6,638	4,205
17	13.277	36,558	6,638	3,772
18	13.277	36,558	6,638	3,384
19	13.277	36,558	6,638	3,035
20	13.277	36,558	6,638	2,723
Expected Total Cost Through the 20th Year Post-Diagnosis for a Bladder Cancer Patient Diagnosed at Age 70				156,670

a. The probabilities used in this table are from Table II.8-3. The costs are from Table II.8-4.

Links to Tables II.8-3 and II.8-4

b. First-year costs include the charge for "initial" therapy ($16,527). The duration of maintenance care is adjusted accordingly (see text for discussion).

c. Calculated using the probabilities in Table II.5-3 and the costs in Columns (2),(3), and (4) of this table.

Link to Table II.5-3

Table II.8-6. Conditional Probabilities of Survival and Mortality for Survivors and Nonsurvivors of Bladder Cancer (Age of Onset = 70)[a]

Years Post-Diagnosis (n)	Bladder Cancer Survivors		Bladder Cancer Nonsurvivors	
	Conditional probability of:		Conditional probability of:	
	Surviving through the *n*th year	Dying of some other cause during the *n*th year	Surviving through the *n*th year	Dying of bladder cancer during the *n*th year
1	.966	.034	.494	.506
2	.934	.033	.451	.043
3	.900	.034	.410	.041
4	.865	.035	.371	.039
5	.828	.036	.334	.037
6	.791	.037	.299	.035
7	.752	.039	.266	.033
8	.713	.040	.234	.031
9	.672	.041	.205	.030
10	.631	.041	.177	.028
11	.589	.042	.151	.026
12	.546	.043	.127	.024
13	.503	.043	.105	.022
14	.459	.044	.085	.020
15	.415	.044	.067	.018
16	.376	.039	.051	.016
17	.341	.035	.036	.015
18	.309	.032	.023	.013
19	.281	.028	.011	.012
20	.255	.025	.000	.011

a. As noted for Table II.8-3, the conditional survival and mortality probabilities for bladder cancer patients presented here are derived from the RSRs estimated from RSRs obtained from NCI and the survival probabilities for a matched cohort in the general population. See Section II.8.A.5.2 for an explanation of the estimation of RSRs.

Link to Section II.8.A.5.2

The expected medical costs for bladder cancer survivors during the first year post-diagnosis may therefore be expressed as:

<u>Expected First-Year Cost:</u> initial treatment costs + [maintenance care costs for nine months × probability of survival through first year + maintenance care costs for three months × probability of dying of other causes during the first year]

The expected medical costs for bladder cancer survivors during the *n*th year post-diagnosis, for *n*>1, then, may be expressed as:

> **<u>Expected *n*th-Year (*n*>1) Cost:</u> [maintenance care cost for one year × probability of survival through *n*th year + maintenance care cost for six months × probability of dying of other causes during the *n*th year]**
>
> **<u>Expected Lifetime Cost</u> = Expected first-year cost + the sum of the (discounted) expected subsequent-year costs**

Note that the probabilities used in these calculations are the conditional probabilities given in Table II.8-6. They are conditional on the bladder cancer patient not dying of bladder cancer.

Using the initial, maintenance, and terminal care costs from Table II.8-6, the mathematical equation for the lifetime costs incurred by bladder cancer survivors is:

$$\$16{,}527 + pm_1^{\,s} \times 0.25\ (\$13{,}277) + ps_1^{\,s} \times .75 \times \$13{,}277 + \sum_{y=2}^{20} \left[ps_y^{\,s} \frac{\$13{,}277}{(1+r)^{y-1}} + pm_y^{\,s} \frac{\$6{,}638}{(1+r)^{y-1}} \right]$$

where:

y	=	the year post-diagnosis;
ps^s	=	the conditional probability of survival for that year, conditional on being a survivor of bladder cancer;
pm^s	=	the conditional probability of mortality for that year, conditional on being a survivor of bladder cancer; and
r	=	the discount rate.

The expected medical costs for bladder cancer survivors for each year post-diagnosis, as well as the expected total medical costs over 20 years post-diagnosis, are shown in Table II.8-7.

Table II.8-7. Expected Undiscounted Costs of Medical Services (in 1996$) for Survivors of Bladder Cancer (Age of Onset = 70)			
	Medical Costs Through the 20th Year Post-diagnosis[a] (undiscounted)		
Years Post-Diagnosis (n)	Medical Cost if Survive Through the *n*th Year	Medical Cost if Die of other Causes in the *n*th Year	Total Cost Based on Weighted Average[b]
1[c]	26,485	19,846	26,262
2	13,277	6,638	12,613
3	13,277	6,638	12,172
4	13,277	6,638	11,713
5	13,277	6,638	11,238
6	13,277	6,638	10,748
7	13,277	6,638	10,243
8	13,277	6,638	9,724
9	13,277	6,638	9,193
10	13,277	6,638	8,649
11	13,277	6,638	8,096
12	13,277	6,638	7,535
13	13,277	6,638	6,965
14	13,277	6,638	6,389
15	13,277	6,638	5,808
16	13,277	6,638	5,255
17	13,277	6,638	4,759
18	13,277	6,638	4,315
19	13,277	6,638	3,916
20	13,277	6,638	3,559
Expected Total (Undiscounted) Cost Through the 20th Year Post-Diagnosis:			**179,153**

a. Costs are based on data reported in Table II.8-4, adapted from Baker et al., 1989. Probabilities of survival and mortality, taken from Table II.8-6, are conditional on surviving bladder cancer.
b. Weighted average of the costs incurred by survivors who survive the year and the costs incurred by survivors who die of other causes during the year. Weighting is based on the conditional probabilities provided in Table II.8-6.
c. Costs during the first year include a charge for "initial" therapy ($16,527), and the duration of maintenance or terminal care is adjusted accordingly. See text for discussion.

II.8.B.1.4.3 Calculation of Lifetime Cost Estimates for Bladder Cancer Nonsurvivors

Nonsurvivors of bladder cancer will incur initial, maintenance, and terminal costs. Their lifetime medical costs associated with the disease can be calculated from the costs per treatment period shown in Table II.8-4 and the conditional probabilities for nonsurvivors of bladder cancer shown in Table II.8-6.

Links to Tables II.8-4 and II.8-6

As Table II.8-6 indicates, about 55 percent of bladder cancer nonsurvivors die within one or two years of diagnosis. Of the remaining 45 percent of nonsurvivors, death from bladder cancer may occur anywhere within the remaining 18 years of the 20-year period considered in this analysis, with the conditional probabilities of death ranging from four percent in the third year post-diagnosis to about one percent in the twentieth year. As with bladder cancer survivors, medical costs for nonsurvivors each year post-diagnosis were calculated as a weighted average of the costs incurred by those who survive the year and those who die (of bladder cancer) during the year.

It was assumed that those who die during a year receive six months of care (as was done for the survivors above). It was also assumed that terminal care lasting six months would be provided to all nonsurvivors. Therefore, unless death occurred during the first year, when initial care was assumed to occur, the care costs assigned to the last year of life were terminal costs. If death occurred during the first year post-diagnosis, it was assumed that initial care and three months (half of the total) of terminal care were provided.

The general description of medical costs for nonsurvivors may be expressed as:

> **Expected First-Year Cost: [initial costs + half the terminal costs] × probability of mortality during the first year + [initial costs + maintenance care costs for nine months] × probability of survival for first year**
>
> **Expected *n*th-Year (*n*>1) Cost: maintenance care cost for one year × probability of survival through *n*th year + terminal costs × probability of mortality in *n*th year**
>
> **Expected Lifetime Cost = Expected first-year cost + the sum of the (discounted) expected subsequent-year costs**

As with the cost calculations for bladder cancer survivors, the probabilities used in these cost calculations are the conditional probabilities given in Table II.8-6, in this case, conditional on dying of bladder cancer.

Link to Table II.8-6

Using the initial, maintenance, and terminal care costs from Table II.8-6, the mathematical equation for the expected lifetime costs incurred by nonsurvivors is:

$$\$16{,}527 + pm_1^{ns} \times 0.5\ (\$36{,}558) + ps_1^{ns} \times .75 \times \$13{,}277 + \sum_{y=2}^{20} \left[ps_y^{ns} \frac{\$13{,}277}{(1+r)^{y-1}} + pm_y^{ns} \frac{\$36{,}558}{(1+r)^{y-1}} \right]$$

where:

y	=	the year post-diagnosis;
ps^{ns}	=	the conditional probability of survival for that year, conditional on being a nonsurvivor of bladder cancer;
pm^{ns}	=	the conditional probability of mortality for that year, conditional on being a nonsurvivor of bladder cancer; and
r	=	the discount rate.

The costs are summed over all years from diagnosis to death. Maintenance care costs are not added in the last year of life because the patient is assumed to receive terminal care during the six months assumed to constitute this period. (The discounted results are shown in the "Results" section that follows.) The approach is the same as that shown in the example in Section II.8.B.1.3. When the costs for each year are summed over a period of 20 years post-diagnosis, the total 20-year cost per nonsurvivor is obtained. These costs are shown in Table II.8-8.

Link to Section II.8.B.1.3

The results shown above can be used to calculate costs for an "average" bladder cancer patient, from the costs calculated for survivors and nonsurvivors. The expected medical costs of a bladder cancer patient can be calculated as a weighted average of the expected costs of survivors and nonsurvivors of bladder cancer. This approach, which was not used to calculate costs for the "average" patient in this chapter, yields the same results as the approach that was shown in Section II.8.B.1.3. In brief, the approach used in this chapter for the average patient (in Section II.8.B.1.3) uses cost data for all patients, weighted by their average utilization of services. If the survivor and nonsurvivor data were used, which incorporate utilization of services, the cost results obtained through separate calculations for the two subgroups are simply re-aggregated based on each group's proportional contribution to the cost. A discussion of why these two approaches yield the same results is provided in Chapter II.2 (Section II.2.B.2.3)

Link to Chapter II.2.B.2.3

Table II.8-8. Expected Undiscounted Costs of Medical Services (in 1996$) for Nonsurvivors of Bladder Cancer (Age of Onset = 70)			
Years Post-Diag-nosis (n)	Medical Costs Through the 20th Year Post-diagnosis[a] (undiscounted)		
	Medical Cost if Survive Through the *n*th Year	Medical Cost if Die in the *n*th Year	Total Cost Based on Weighted Average[b]
1[c]	26,485	34,806	30,699
2	13,277	36,558	7,543
3	13,277	36,558	6,936
4	13,277	36,558	6,352
5	13,277	36,558	5,793
6	13,277	36,558	5,264
7	13,277	36,558	4,750
8	13,277	36,558	4,261
9	13,277	36,558	3,797
10	13,277	36,558	3,359
11	13,277	36,558	2,955
12	13,277	36,558	2,564
13	13,277	36,558	2,200
14	13,277	36,558	1,862
15	13,277	36,558	1,551
16	13,277	36,558	1,274
17	13,277	36,558	1,016
18	13,277	36,558	784
19	13,277	36,558	577
20	13,277	36,558	390
Expected Total (Undiscounted) Cost Through the 20th Year Post-Diagnosis:			**93,927**

a. Costs are based on data reported in Table II.8-4, adapted from Baker et al., 1989. Probabilities of survival and mortality, taken from Table II.8-6, are conditional on dying of bladder cancer within 10 years post-diagnosis.

Links to Tables II.8-4 and II.8-6

b. Weighted average of costs incurred by nonsurvivors who survive the year and those who die during the year. Weighting is based on the conditional probabilities shown in Table II.8-6.

c. Costs during the first year include "Initial" therapy ($16,527) , and pro-rated maintenance or terminal care. See text for discussion.

II.8.B.2. Results of Medical Cost Analysis

The per-patient lifetime direct medical costs calculated for the "average" bladder cancer patient (as shown in Table II.8-5), bladder cancer survivors (as shown in Table II.8-7) and bladder cancer nonsurvivors (as shown in Table II.8-8) diagnosed at age 70 are listed in Table II.8-9. Undiscounted costs and costs discounted at three, five, and seven percent back to year

one (time of diagnosis) are shown.[12] Discounting was carried out for 20 years following diagnosis and comprises the assumed full duration of maintenance care for survivors.

Links to Tables II.8-5 and II.8-7

Table II.8-9. Incremental Per-capita Medical Costs for the Average Bladder Cancer Patient, Survivors, and Nonsurvivors (Diagnosed at Age 70) Undiscounted and Discounted at 3, 5, and 7 Percent ($1996)

	Discount Rate			
Patient Group	**Undiscounted**	**3**	**5**	**7**
Survivors	$179,153	$148,149	$132,653	$120,132
Nonsurvivors	$93,927	$83,449	$77,983	$73,424
Average Patient	$156,670	$131,081	$118,231	$107,811

See text for a definitions of patient groups.

The costs presented in this chapter were current in the year the chapter was written. They can be updated using inflation factors accessible by clicking below.

Link to inflation factors

The results show substantially higher costs for survivors than nonsurvivors, due primarily to their ongoing maintenance care. It is noted that although a 20-year maintenance period for bladder cancer survivors is assumed (with adjustment for background mortality that reduces utilization), the actual average period of maintenance is not known. Maintenance periods are likely to vary considerably among individuals, depending on age, health status, access to care, and other factors. Maintenance care costs comprise the major cost element in determining the "average" patient costs, due to the relatively low mortality attributable to bladder cancer. The uncertainty surrounding the period of maintenance care for survivors could therefore have an impact on the cost estimates for the "average" patient and for survivors of bladder cancer. Because less than half of bladder cancer patients diagnosed at age 70 survive beyond the first ten years post-diagnosis (most die of causes other than bladder cancer), the impact of maintenance care costs on the costs of the "average" 70-year-old patient is less than it would be if there were a lower overall mortality rate (i.e., if diagnosis occurred at younger ages).

[12] As noted previously, costs will be higher if ages of diagnosis are earlier. The uncertainty analysis in Section II.8.C contains additional cost estimates for earlier ages of diagnosis.

II.8.B.3. Other Studies

A number of other studies were reviewed for this analysis. Most had shortcomings with respect to the duration of the study (e.g., only one year of medical cost data obtained) or the age of the data. A select group of these are discussed below.

II.8.B.3.1 Hartunian et al.

Hartunian et al.'s (1981) method of estimating the costs of illness has been discussed in Chapter I.1. The authors defined expected treatment on a yearly basis, developed annual costs of the treatment, and combined the cost data with survival data. Using this method, they estimated the costs of cancer at eight sites, including cancer of the urinary system, which includes bladder, kidney, and related structures.

Link to Chapter I.1

Hartunian et al. estimated the costs of inpatient stays using a 1976 study by Scotto and Chazze of newly diagnosed cancer patients followed over a two-year period to establish hospitalization and payment patterns. These data were supplemented by questionnaire data. The Hartunian data are quite old (over 20 years) and both survival and treatment methods have changed since that time. Their estimated survival for bladder cancer was 0.15 percent, which is considerably lower than the current survival statistics and impacts the percentage of patients who access care components (reducing medical cost estimates through high death rates). Medical treatment has also changed considerably since their data were obtained. In addition, they also limit their analysis to two years post-diagnosis, which is not sufficient due to both the prolonged period of detailed follow up care that is required (note the 20 year post-diagnosis time frame for increased mortality) and the frequency of relapse.

II.8.B.3.2 Riley et al.

A study of Medicare payments from diagnosis to death in elderly cancer patients was carried out by Riley et al. (1995). The cost estimates are based on Medicare payments only, which do not include: most nursing home care, home health care, pharmaceuticals unless supplied for inpatients, out-of-pocket expenses, deductibles, charges in excess of Medicare paid by other sources (e.g., coinsurance), and other related medical services not covered by Medicare.

Medicare patients younger than 65 were not included and the average age at diagnosis of the bladder cancer cohort was 75.2 years, in contrast with the 70 year national average. Riley et al. note that patients diagnosed at younger ages have higher costs. In addition, those diagnosed at earlier stages have a better prognosis but may have higher medical costs (due to longer continuing care).

Medical costs are reported for all patients who were diagnosed with bladder cancer, regardless of other diseases or their ultimate causes of death. Due to the links among bladder cancer, smoking, and numerous other diseases, this method is especially problematic because costs associated with other illnesses may be commingled with the bladder cancer costs.

The background cost per year for medical services was estimated by Riley et al. to be $2,250 ($3,154 in 1996 dollars), based on the experience of all people over the age of 65 who received Medicare-compensated care. The study excluded those costs that occur during the last year of a person's life. Consequently, the estimated background value may underestimate background costs, especially as age and associated mortality risks increase over the age of 65.

Riley et al. estimated that the total average Medicare payment from diagnosis to death for persons diagnosed with bladder cancer was $57,629 in 1990 dollars, adjusted to $80,796 in 1996 dollars (CPI 1990:1996 = 1.402). This estimate is considerably lower than those obtained from Baker et al. The difference is most likely due to the exclusion of many costs not covered by Medicare, and the various other factors described above that tend to reduce the cost estimate. Due to these limitations, the Riley et al. study is not recommended for a benefits evaluation.

II.8.C. Uncertainties and Limitations

As noted periodically in the above discussion, there is uncertainty surrounding various aspects of the analysis. Information concerning some inputs to the analysis was limited. Although a complete uncertainty analysis is beyond the scope of this work, the significant sources of uncertainty are discussed. Limitations of the scope of the analysis are also discussed.

II.8.C.1. Uncertainties Surrounding Key Inputs to the Analysis

II.8.C.1.1. Analysis of Medical Costs

The cost estimates based on Baker et al. (1989, 1991) have a number of limitations, many of them noted by Baker et al. (1991), Mor et al. (1990), and Mor (1993). Most of these limitations arise from the use of CMHSF. Medicare data have five limitations that decrease its value for calculating the average lifetime direct medical costs of treating bladder cancer. First, Medicare covers medical services only for most persons age 65 and over, disabled persons entitled to Social Security cash benefits for at least 24 months, and most persons with end-stage renal disease. All patients not covered by Medicare are excluded from the database, including all non-

disabled women under 65, and women over 65 using private health insurance (Baker et al., 1991).

Given that diagnosis of bladder cancer occurs in almost half of all patients before age 65, the CMHSF excludes a significant number of younger patients. According to Mor et al., treatment for younger women for other cancers tends to be more intensive (and therefore more costly per unit time) than treatment for older women, though older women tend to have longer hospital stays. This is likely to be the case for bladder cancer as well, and may be supported by the improved cancer-specific five-year survival observed among younger versus older patients. Because these differences counteract each other, the omission of younger patients from the Baker et al. analysis is not expected to affect the results substantially. In addition, the majority of senior citizens are enrolled in Medicare (Ibid); differences in medical costs incurred by senior citizens not using Medicare should have little effect on overall cost estimates.[13]

Medicare also does not cover self-administered drugs, intermediate nursing care, long-term nursing care, and some expensive new treatments (such as bone marrow transplants). For some patients, these costs may represent significant percentages of total treatment costs. Most direct medical costs, however, appear to be covered by the CMHSF database and are included in Baker et al.'s analysis. In addition, Baker et al. made adjustments for some cost elements not covered by Medicare (see Section II.8.B).

Another drawback is that Baker et al. were not able to identify bladder cancer patients in CMHSF whose diagnosis and first course of therapy did not involve hospitalization. In an analysis of Rhode Island non-bladder cancer patients covered by Medicare, Mor et al. determined that a small percentage of patients were initially diagnosed without hospitalization, and had substantially lower initial and subsequent treatment costs (Mor et al., 1990). This omission likely causes average treatment costs to be overestimated, though by relatively little.

A fourth drawback is that Baker et al. (1989) provide no information concerning the duration of the maintenance period for bladder cancer. The analysis in this chapter considers a 20-year period. If the average duration of maintenance care among patients of bladder cancer is shorter (longer) than 20 years, the estimates of the costs incurred would be biased upward (downward). This function is true for survivors as well as nonsurvivors of bladder cancer.

[13] This figure represents those enrolled in Medicare Part A; 95 percent of those enrolled in Medicare Part A choose also to enroll in Medicare Part B.

A fifth drawback is that the data used by Baker are from the period 1974 to 1981, leading to uncertainty regarding changes in treatment methods and costs.

Finally, the reliability of the data contained in the database used by Baker et al. varies. An independent analysis of CMHSF performed in 1977 by the Institute of Medicine of the National Academy of Sciences found that the frequency of discrepancies in principal diagnoses varied among diseases (Baker et al., 1991). It is unclear whether the presence of misnamed diagnoses contained in CMHSF potentially increases or decreases the resultant cost estimates.

Overall, despite the limitations described above, Baker's analysis of the CMHSF data represents the most nationally-representative, per-patient lifetime estimate of the direct medical costs of treating bladder cancer to date. Their cost estimates are based on sound criteria. Some of the data limitations underestimate costs, and others overestimate costs; the sum of the data limitations therefore decreases the magnitude of error. More of the uncertainties in their analysis appear to underestimate costs, however; the net result is a likely underestimation of actual direct medical costs. Although there are some uncertainties associated with the estimation of the survival and mortality probabilities used in the calculation of expected medical costs (discussed below), these uncertainties are likely to be relatively small. As noted in the text, NCI RSRs used to estimate survival and mortality for this analysis are based on the survival experience of a large group of bladder cancer patients considered in relation to the survival experience of the general population.

An additional limitation of this analysis is that medical costs incurred as a result of bladder cancer, but not considered by Baker et al., may arise as a result of treatment for bladder cancer. Secondary cancers and other adverse health effects may occur due to radiation, chemotherapy treatment, and other therapies. These effects may occur substantially after bladder cancer treatment has been completed and can incur added medical costs not considered in this chapter. Many concurrent and related costs are included, however, due to the methods used by Baker et al. The authors considered all costs due to any medical services, minus the background costs of all individuals who did not have cancer.

As with all chronic diseases, it is difficult to estimate the period following diagnosis and initial treatment, during which additional medical monitoring and follow-up care take place. Data have not yet been located regarding the average duration of maintenance care for bladder cancer. For purposes of this analysis, 20 years of follow-up care was assumed to be reasonable, due to the severity of the disease and the consequences of bladder surgery.

As noted above, there is a prolonged period during which mortality continues to increase, indicating that morbidity must be monitored for many years post-diagnosis. The estimated time required for maintenance care may be revised in the future if data are located.

There is additional uncertainty associated with the age of onset of the disease and the resulting medical costs. If bladder cancer is induced at an earlier than average age (70 years), as may be the case with arsenic-induced bladder cancer if it follows the skin cancer pattern, the direct medical costs will be greater, particularly the maintenance costs. Younger patients will survive to require medical treatment and follow-up for a longer period (on average) than those who are diagnosed at age 70, because they have fewer competing causes of death. In addition, bladder cancer frequently recurs and patients require careful monitoring; some require treatment for recurrent cancer. The latter is more likely with young patients who may survive for many decades after initial diagnosis.

II.8.C.2. Scope of the Analysis

The analysis in this chapter was confined to direct medical costs by the patient. As noted in Chapter I.1, willingness-to-pay has many other cost elements.

Link to Chapter I.1

The analysis does not include time lost by the patient or their family and friends who provide care. Also omitted from cost of illness estimates are pain and suffering on the part of the patient or their family and friends, changes in job status among previously employed patients, training for new job skills due to physical limitations, or medical costs incurred after the 20-year maintenance period. These cost elements may comprise a substantial portion of the total cost of bladder cancer.